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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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MAY 0 6 2002

Office Action Summary

Application No.	Applicant(s)	
09/709,691	FOLDVARI ET AL.	
Examiner	**Art Unit**	
Robert M DeWitty	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

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1)☒ Responsive to communication(s) filed on *18 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *30-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-29, drawn to a composition, classified in class 424, subclass 450.

   II. Claims 30-46, drawn to methods of use, classified in class 514, subclass 54.

2. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the method of treating using IFN-alpha can be practiced using another materially different product, such as oral compositions or injections.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

Claim 1 is generic to a plurality of disclosed patentably distinct species comprising interferon-alpha, a phospholipid, and a fatty acylated amino acid. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for interferon-alpha,

a phospholipid, and a fatty acylated amino acid, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Judy Mohr on August 28, 2001 and again on September 4, 2001, a provisional election was made with traverse to prosecute the invention of Group 1, claims 1-29, species IFN-alpha$_{2b}$, phosphatidylcholine, and PDMb27. Affirmation of this election must be made by applicant in replying to this Office action. Claims 30-46 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari et al. (U.S. Pat. No. 5,993,852), further in view of Foldvari et al. (Dermal and

transdermal delivery of protein pharmaceuticals: lipid-based delivery systems for interferon-alpha).

Foldvari (**852) teaches the transdermal administration of vaccine composition comprised of lipid vesicles. Foldvari teaches that vaccines can be administered by injection or orally, however administration by injection is not always a convenient method (col. 2, lines 6-9). The composition as taught of Foldvari can be comprised of a suspension of biphasic lipid vesicles having a central core compartment containing an oil-in-water emulsion, entrapped in the biphasic lipid vesicles.

The biphasic lipid vesicles are multilamellar lipid vesicles composed of a series of lipid bilayers (col. 4, lines 36-39). The innermost bilayer in the vesicle defines a central core compartment containing an oil-in-water emulsion. The oil-in-water emulsion is entrapped in the lipid vesicles by preparing a surfactant-stabilized oil-in-water emulsion. The emulsion is mixed with vesicle-forming lipids to form lipid bilayers around the emulsion (col. 4, lines 46-56).

The lipid components necessarily include a vesicle-forming lipid, such as naturally-occurring lipids such as phosphatidylcholine (col. 6, line 15).

In one embodiment, the biphasic lipid vesicles include a permeation enhancer to enhance the penetration of the immunogen (or antigen). In preferred embodiments, the permeation enhancer is a fatty acylated amino acid, such as monolauroyllysine or dipalmitoyllysine (col. 8, lines 19-27).

However, Foldvari (**852) does not teach the incorporation of IFN-alpha into the composition for transdermal administration.

Foldvari (Dermal and transdermal delivery of protein pharmaceuticals) teaches the encapsulation of drugs such as IFN-alpha for transdermal delivery. It is taught that the prior art showed that delivery of IFN-alpha from various topical dosage forms such as gels and creams resulted in either negative or positive results. It is postulated that the lack of efficacy was the result of poor delivery of the drug (page 130, column 1). It is taught that a strategies to improve absorption of such drugs include encapsulation, and the use of penetration enhancers (page 129, col. 2). In an example, IFN-alpha2b was encapsulated, and applied to the skin to measure transdermal uptake of the drug. Results show that liposome encapsulation increased cutaneous delivery of IFN-alpha (page 136, col. 1). It was further disclosed that liposome encapsulation, while showing immediate clinical application, was further improved using a third-generation of lipid-based delivery systems (biphasic delivery system) (Id.).

Based on the art available at the time the invention was made, a biphasic delivery system comprised of lipid vesicles and entrapped IFN-alpha would have been known to one of ordinary skill in the art. Motivation to make such biphasic delivery system would have arisen in order to administer IFN-alpha in an another method than injection. Further motivation would have arisen in order to increase the uptake of IFN-alpha by the skin. Further still, it is taught that liposome encapsulation of IFN-alpha can be improved using biphasic delivery systems.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. DeWitty whose telephone number is 703-308-2411. The examiner can normally be reached on 9:00am - 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4527. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

RMD
September 4, 2001